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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/609,417	07/01/2003	Denis Leclerc	1398-104US	9472

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/609,417	LECLERC ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-25 and 27-58* is/are pending in the application.

4a) Of the above claim(s) *31 and 40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-25,27-30,32-39 and 42-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/8/2008 and 3/7/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed January 8, 2008 in response to the Office Action of September 11, 2007 is acknowledged and has been entered. Claims 20, 25, 27, 43, 44, 48, and 56-58 are amended. Claims 20-25, 27-30, 32-39, and 42-58 are under examination.

Information Disclosure Statement

The information disclosure statements filed 3/7/20008 and 1/8/2008 have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 20-25, 27-30, 32-39, and 42-58 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is maintained.**

Applicant's arguments have been fully considered but fail to persuade. Applicants amended the claims to recite: "(...) genetically modified PapMV coat protein being capable of assembling to form said VLP, wherein said genetically modified coat protein comprises one or more amino acid deletions, insertions and/or substitutions (...)". Applicants argue that cloning and generation of various modified PapMV capsid proteins had been described in the art. Applicants cite references by Lee-Shanok, Ikegami and others disclosing generation of a number of recombinant mutant PapMV capsid proteins comprising amino acid deletions, insertions and frame shit mutations. Applicants argue that at the time when the instant Application was filed protein engineering was well established art and that modifications that could be made to a

known protein sequence without affecting the protein function were well understood by the skilled artisan. Applicants further argue that information relating to the genetic modification of proteins, including PapMV protein, was available at the time the instant application was filed, and thus Applicants assert that there is no requirement for such information to be described in detail in the present specification.

In response to Applicant's arguments the Office agrees that that cloning and generation of various modified PapMV capsid proteins had been described in the art. The references mentioned by Applicants, Lee-Shanok and Ikegami are cited in the art rejection below. The Office does not question the level of expectation of success of making modified PapMV protein as long as the skilled artisan receives guidance with respect to what specific modifications should be made, and what specific functions should the modifications result in. In the present case the question is whether the Applicant was in possession of the invention as claimed. The current claims broadly encompass a genus of modifications, while the specification does not disclose a single species of a deletion, insertion or substitutions of the amino acids within the PapMV capsid protein. The references by Lee-Shanok, Ikegami, and Trembley specifically disclose substitutions and deletions of particular amino acids within the PapMV coat protein. The art does not disclose amino acid insertions encompassed by the claims. It is acknowledged that claims recite the function such as "assembling to form said VLP". However because of the absence of a representative number of species (such as specific structures of modified PapMV proteins, for example particular amino acids being mutated or deleted) for the claimed genus in the specification it is determined that Applicants were not in possession of the claimed invention. Therefore the rejection is maintained.

New Rejection

The reference by Lee-Shanok cited in the rejection U.S.C. 35 103(a) below was cited in the art rejection (presently withdrawn) under U.S.C. 35 102(b) in the Office Action of September 11, 2007. The secondary reference by Ikegami cited in the rejection below was submitted by the Applicants in the IDS of June 8, 2005, before the issuance of the first Office Action, however the reference was not considered due to poor legibility. In the IDS of January 8, 2008 Applicants submitted a legible copy of the Ikegami reference. The present Office Action is made non-final because Applicants submitted the cited reference prior to the first Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-25, 27-30, 32-39, 42-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee-Shanok (Thesis for Degree of Master of Science, University of Toronto, 1999) in view of Ikegami (Thesis for Degree of Master of Science, University of Toronto, 1995 in IDS of 1/8/2008).

Claims are drawn to a method of potentiating an immune response against an antigen comprising B-cell antigenic and/or T-cell antigenic epitopes, the method comprising the step of administering to an animal an antigen and an effective amount of an adjuvant, wherein said adjuvant is a papaya mosaic virus (PapMV) or a virus-like particle comprising PapMV coat

protein or modified PapMV coat protein, wherein the antigen is not linked to said PapMV or VLP, or is fused or covalently attached to a coat protein of PapMV at a location other than N-terminus, such that said antigen is disposed on the outer surface of the PapMV or VLP.

The PapMv is a wild type virus, a recombinant virus, and a pseudovirus. The antigen, specifically the hepatitis C virus antigenic epitope is covalently attached to PapMV or VLP, the PapMV or VLP and the antigen are not linked. The antigen together with the PapMV adjuvant are administered orally. The immune response is a humoral and a cellular immune response. With regard to the limitation of pseudoviruses the current specification discloses that pseudoviruses are included in the papaya mosaic virus VLP. Without specific definition in the current specification with regard to pseudoviruses it is understood that pseudoviruses are encompassed within the claimed modified papaya mosaic virus VLPs. Claims are drawn to a method comprising the step of administering to an animal an antigen and an effective amount of an adjuvant, wherein said adjuvant is a papaya mosaic virus (PapMV) or a virus-like particle comprising PapMV coat protein or modified PapMV coat protein. The adjuvant is administered to an animal prior to administration of the antigen and the adjuvant is administered subsequence to administration of the antigen.

Lee-Shanok teaches a method of potentiating an immune response against antigenic epitopes, specifically HCV epitopes recombinantly engineered to be expressed by papaya mosaic virus like particles (see the entire document, particularly the Results on pages 52, 55-58, 72, and Figure 5). The papaya mosaic virus taught by Lee-Shanok has been genetically modified (see Abstract and Results). Lee-Shanok teaches purified wild-type PapMV VLP (see pages 83-84 and Figure 16). Lee-Shanok teaches oral administration of the papaya mosaic virus particles fused

with the HCV epitope (see page 91). Lee-Shanok does not specify what kind of immune responses are generated due to administration of papaya mosaic virus particles fused with the HCV nucleocapsid gene, however Lee-Shanok discloses that papaya mosaic virus particles fused with the HCV nucleocapsid gene can be used as a vaccine (see pages 90-92). Because Lee-Shanok broadly refers to the immune responses, it is expected that humoral and cellular immune responses are generated in the method disclosed by Lee-Shanok.

Lee-Shanok does not teach particular immunization schedule currently claimed, however it would have been well within the knowledge and ability of the ordinary artisan to implement various immunization schedules including changing the order of antigen versus adjuvant being administered. One of ordinary skill would have been motivated to administer an adjuvant prior to administration of an antigen and vise-versa for the purpose of optimizing the immunization effect. Thus the current invention is unpatentable as being obvious over the prior art and the general knowledge in the art of vaccine development.

It is noted that claims 57 and 58 are viewed as product by process claims, and do not further limit the method steps of the claimed invention.

Lee-Shanok further teaches fusion of the foreign antigens to the PapMVcoat protein of the papaya mosaic virus particles (see pages, 32, 52, and 90). While Lee-Shanok teaches the fusion of the HCV antigens to the N-terminus of the PapMV coat protein, Lee-Shanok does not expressly teach fusion of the antigens at a location other than N-terminus such that the antigen is disposed on the outer surface of the PapMV or VLP.

However in view of the teaching of Ikegami, it would have been obvious to fuse or covalently attach foreign antigens at a location other than N-terminus, such as for example at the

C-terminus of the PapMV coat protein (as required by claim 48 and 56 and broadly encompassed by claim 20), because Ikegami teaches that the N- and C-terminal regions of the potexivirus coat protein are exposed to the outer surface of the assembled viral particles (see pages 128 and 131), (it is noted that papaya mosaic virus belongs to the potexivirus family). One would have been motivated to fuse foreign antigens at the C-terminus of the PapMV coat protein because the fusion of the foreign antigens at the C-terminus of the PapMV coat protein would facilitate the antigens to be disposed on the outer surface of the PapMV.

One would have had a reasonable expectation of success to fuse an antigen to the C-terminus of the PapMV because the recombinant technology techniques required for making protein fusion have been known and established in the art at the time of the present invention.

Thus the present claims would have been *prima facie* obvious to the skilled artisan at the time when the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on Monday – Friday 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Agnieszka Boesen, Ph.D./
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648